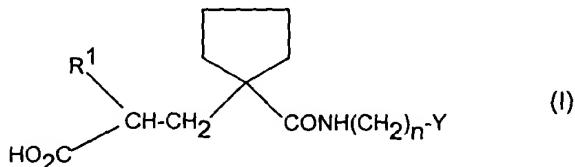


Claims

1 A method of treating female sexual dysfunction comprising administering a therapeutically effective amount of a compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof:

5



wherein

R¹ is C₁-6alkyl which may be substituted by one or more substituents, which may

be the same or different, selected from the list: halo, hydroxy, C₁-6

10 alkoxy, C₂-6 hydroxyalkoxy, C₁-6 alkoxy(C₁-6alkoxy), C₃-7cycloalkyl, C₃-7cycloalkenyl, aryl, aryloxy, (C₁-4alkoxy)aryloxy, heterocyclyl,

heterocyclyloxy, -NR²R³, -NR⁴COR⁵, -NR⁴SO₂R⁵, -CONR²R³,

-S(O)_pR⁶, -COR⁷ and -CO₂(C₁-4alkyl); or R¹ is C₃-7cycloalkyl, aryl or

heterocyclyl, each of which may be substituted by one or more

15 substituents from said list, which substituents may be the same or

different, which list further includes C₁-6alkyl; or R¹ is C₁-6 alkoxy,

-NR²R³ or -NR⁴SO₂R⁵;

wherein

R² and R³ are each independently H, C₁-4alkyl, C₃-7cycloalkyl (optionally

20 substituted by hydroxy or C₁-4alkoxy), aryl, (C₁-4alkyl)aryl, C₁-

6alkoxyaryl or heterocyclyl; or R² and R³ together with the nitrogen to

which they are attached form a pyrrolidinyl, piperidino, morpholino,

piperazinyl or N-(C₁-4 alkyl)piperazinyl group;

R⁴ is H or C₁-4alkyl;

25 R⁵ is C₁-4alkyl, CF₃, aryl, (C₁-4 alkyl)aryl, (C₁-4alkoxy)aryl, heterocyclyl,

C₁-4alkoxy or -NR²R³ wherein R² and R³ are as previously defined;

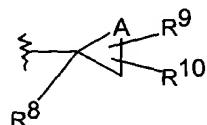
R⁶ is C₁-4alkyl, aryl, heterocyclyl or NR²R³ wherein R² and R³ are as previously

defined; and

R⁷ is C₁₋₄alkyl, C₃₋₇cycloalkyl, aryl or heterocycl; p is 0, 1, 2 or 3; n is 0, 1 or 2; the -(CH₂)_n- linkage is optionally substituted by C₁₋₄alkyl, C₁₋₄alkyl substituted with one or more fluoro groups or phenyl, C₁₋₄alkoxy, hydroxy, hydroxy(C₁₋₃alkyl), C₃₋₇cycloalkyl, aryl or heterocycl;

5

Y is the group



wherein A is -(CH₂)_q- where q is 1, 2, 3 or 4 to complete a 3 to 7 membered carbocyclic ring which may be saturated or unsaturated; R⁸ is H, C₁₋₆alkyl, -CH₂OH, phenyl, phenyl(C₁₋₄alkyl) or CONR¹¹R¹²; R⁹ and R¹⁰ are each independently H, -CH₂OH, -C(O)NR¹¹R¹², C₁₋₆alkyl, phenyl (optionally substituted by C₁₋₄alkyl, halo or C₁₋₄alkoxy or phenyl(C₁₋₄alkyl) wherein the phenyl group is optionally substituted by C₁₋₄alkyl, halo or C₁₋₄alkoxy, or R⁹ and R¹⁰ together form a dioxolane; R¹¹ and R¹² which may be the same or different are H, C₁₋₄alkyl, R¹³ or S(O)_rR¹³, where r is 0, 1 or 2 and R¹³ is phenyl optionally substituted by C₁₋₄alkyl or phenylC₁₋₄alkyl wherein the phenyl is optionally substituted by C₁₋₄alkyl; or

10

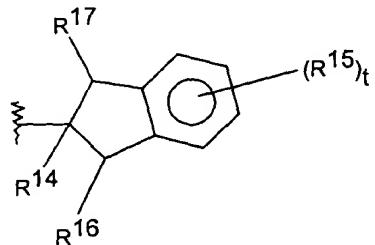
Y is the group, -C(O) NR¹¹ R¹² wherein R¹¹ and R¹² are as previously defined except that R¹¹ and R¹² are not both H; or

15

Y is the group, -C(O) NR¹¹ R¹² wherein R¹¹ and R¹² are as previously defined except that R¹¹ and R¹² are not both H; or

20

Y is the group,



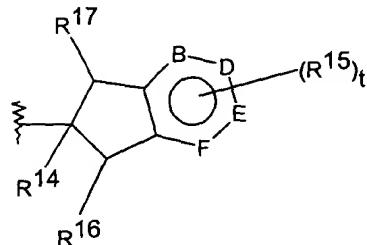
wherein R¹⁴ is H, CH₂OH, or C(O)NR¹¹R¹² wherein R¹¹ and R¹² are as

25

previously defined; when present R¹⁵, which may be the same or different

to any other R¹⁵, is OH, C₁₋₄alkyl, C₁₋₄alkoxy, halo or CF₃; t is 0, 1, 2, 3 or 4; and R¹⁶ and R¹⁷ are independently H or C₁₋₄ alkyl; or

Y is the group



5 wherein one or two of B, D, E or F is a nitrogen, the others being carbon; and
 R¹⁴ to R¹⁷ and t are as previously defined; or

Y is an optionally substituted 5-7 membered heterocyclic ring, which may be
 saturated, unsaturated or aromatic and contains a nitrogen, oxygen or
 sulphur and optionally one, two or three further nitrogen atoms in the ring
 and which may be optionally benzofused and optionally substituted by:
 10 C₁₋₆ alkoxy; hydroxy; oxo; amino; mono or di-(C₁₋₄alkyl)amino;
 C₁₋₄alkanoylamino; or
 C₁₋₆alkyl which may be substituted by one or more substituents, which may be
 the same or different, selected from the list: C₁₋₆alkoxy, C₁₋₆haloalkoxy,
 15 C₁₋₆alkylthio, halogen, C₃₋₇cycloalkyl, heterocyclyl or phenyl; or
 C₃₋₇cycloalkyl, aryl or heterocyclyl, each of which may be substituted by one or
 more substituents, which may be the same or different, selected from the
 list: C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy, C₁₋₆alkylthio, halogen, C₃₋₇cycloalkyl, heterocyclyl or phenyl;

20 wherein when there is an oxo substitution on the heterocyclic ring, the ring only
 contains one or two nitrogen atoms and the oxo substitution is adjacent a
 nitrogen atom in the ring; or
 Y is -NR¹⁸S(O)_uR¹⁹, wherein R¹⁸ is H or C₁₋₄alkyl; R¹⁹ is aryl, arylC₁₋₄alkyl or
 heterocyclyl; and u is 0, 1, 2 or 3.

25 2 A compound of formula (I), pharmaceutically acceptable salts, solvates,
 polymorphs or prodrugs thereof, wherein R¹, n and Y are as defined in claim 1
 with the proviso that Y is not the group -C(O)NR¹¹R¹² and when R¹ is propyl or
 phenylethyl, R¹⁴ is not -CH₂OH.

3 A compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹, n and Y are as defined in claim 1 with the proviso that Y is not the group -C(O)NR¹¹R¹² and R¹⁴ is not H or

5 -CH₂OH.

4 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹ is C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(C₁₋₃)alkyl, C₁₋₆alkoxyC₁₋₆alkoxyC₁₋₃alkyl or C₁₋₆alkyl substituted with aryl.

5 A compound according to claim 4, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹ is C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(C₁₋₃)alkyl or C₁₋₆alkoxyC₁₋₆alkoxyC₁₋₃alkyl.

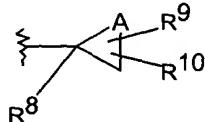
6 A compound according to claim 5, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹ is C₁₋₄alkyl or

20 C₁₋₆alkoxy(C₁₋₃)alkyl.

7 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is the group

25 and the carbocyclic ring is fully saturated, then preferably one of R⁹ or R¹⁰ is -CH₂OH; -C(O)NR¹¹R¹²; C₁₋₆alkyl; phenyl optionally substituted by C₁₋₄alkyl; or phenyl(C₁₋₄alkyl) wherein the phenyl group is optionally substituted by C₁₋₄alkyl.

30 8 A compound according to claim 7, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the carbocyclic ring is 5, 6 or 7



membered wherein one of R⁹ or R¹⁰, is -C(O)NR¹¹R¹², with the other being C₁₋₆alkyl; phenyl optionally substituted by C₁₋₄alkyl; or phenyl(C₁₋₄alkyl) wherein the phenyl group is optionally substituted by C₁₋₄alkyl.

5 9 A compound according to claim 7, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R⁹ and R¹⁰ are attached to adjacent carbon atoms in the ring.

10 10 A compound according to claim 7 pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R⁸ is CH₂OH.

11 11 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is the group -NR¹⁸S(O)_uR¹⁹, preferably R¹⁸ is H.

15 12 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹⁹ is benzyl or phenyl.

13 20 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein u is 2.

14 25 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is an optionally substituted 5-7 membered heterocyclic ring.

15 30 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is an optionally substituted aromatic ring.

16 35 A compound according to claim 15, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein said aromatic ring is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, triazolyl, tetrazolyl, oxadiazolyl, thiazolyl, thiadiazolyl, oxazolyl, isoxazolyl, indolyl, isoindolinyl, quinolyl, isoquinolyl, pyridonyl, quinoxalinyl or quinazolinyl each of which may be substituted as defined in claim 1.

17 A compound according to claim 16, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is oxadiazole, pyridone or thiadiazole each of which may be substituted as defined in claim 1.

5

18 A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is 1,2,5-oxadiazole, 1,3,4-oxadiazole, 2-pyridone or 1,3,4-thiadiazole each of which may be substituted as defined in claim 1.

10

19 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by one or more C₁₋₆alkyl, phenyl or phenylC₁₋₄alkyl.

15

20 A compound according to claim 19, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by C₁₋₄alkyl or benzyl.

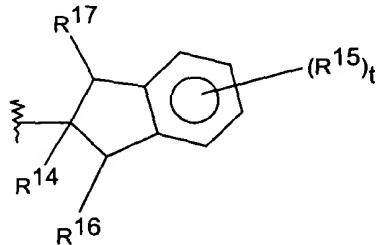
21

20 A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is a pyridone said pyridone is N-substituted pyridone.

22

25 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is a lactam linked at the nitrogen.

23 A compound according to any claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is

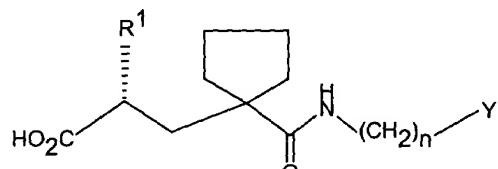


30 wherein R¹⁴ is CH₂OH or C(O)NR¹¹R¹²

24 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹⁶ and R¹⁷ are hydrogen.

25 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein t is 0.

26 A compound of formula Ie, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof,



10 (Ie)
wherein R¹, Y and n are as defined in claim 2.

27 A compound, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, selected from the group consisting of:

15 2-[(1-{{(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino]carbonyl}cyclopentyl}-methyl]-4-methoxybutanoic acid;

2-{{1-{{(3-(2-oxo-1-pyrrolidinyl)propyl)amino]carbonylcyclopentyl}-methyl}-4-phenylbutanoic acid);

(+)-2-{{1-{{(2-hydroxymethyl)-2,3-dihydro-1H-inden-2-yl]amino}carbonyl)cyclopentyl)methyl}-4-phenylbutanoic acid;

20 2-[(1-{{(5-methyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)methyl]-4-phenylbutanoic acid;

cis-3-(2-methoxyethoxy)-2-[(1-{{(4-{{(phenylsulfonyl)amino]carbonyl}cyclohexyl)-amino]carbonyl}cyclopentyl)methyl]propanoic acid;

25 (+)-2-{{1-{{(2-hydroxymethyl)-2,3-dihydro-1H-inden-2-yl]amino}carbonyl)cyclopentyl}-methyl}pentanoic acid;

(2R)-2-[(1-{{(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid or (-)-2-[(1-{{(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid;

30 (2S)-2-[(1-{{(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid or (+)-2-[(1-{{(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid ;

2-({1-[(3-benzylanilino)carbonyl]cyclopentyl}methyl)pentanoic acid ;
2-[(1-{{(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino}carbonyl}cyclopentyl)-
methyl]pentanoic acid ;
2-{{1-((1R,3S,4R)-4-(aminocarbonyl)-3-butylcyclohexyl)amino}carbonyl}-
5 cyclopentyl]methyl]pentanoic acid ;
trans-3-[1-{{[2-(4-chlorophenyl)cyclopropyl]amino}carbonyl}cyclopentyl]-2-
(methoxymethyl)propanoic acid ;
trans-3-[1-{{[2-(4-methoxyphenyl)cyclopropyl]amino}carbonyl}cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
10 *trans*-3-[1-{{[2-pentylcyclopropyl]amino}carbonyl}cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
3-[1-{{[5-benzyl-[1,3,4]-thiadiazol-2-yl]amino}carbonyl}cyclopentyl]-2-
15 (methoxyethyl)propanoic acid ;
3-[1-{{[4-butylpyridin-2-yl]amino}carbonyl}cyclopentyl]-2-(methoxyethyl)propanoic
acid ;
3-[1-{{[4-phenylpyridin-2-yl]amino}carbonyl}cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
3-[1-{{[1-hydroxymethyl-3-phenylcyclopentyl]amino}carbonyl}cyclopentyl]-2-
20 (methoxyethyl)propanoic acid ;
2-{{1-{{[2-(hydroxymethyl)-2,3-dihydro-1H-inden-2-yl]amino}carbonyl}-
cyclopentyl}methyl}-4-methoxybutanoic acid ;
trans-3-[1-{{[2-phenylcyclopropyl]amino}carbonyl}cyclopentyl]-2-
25 (methoxyethyl)propanoic acid ;
(*R*)- 2-{{1-{{[2-(hydroxymethyl)-2,3-dihydro-1H-inden-2-yl]amino}carbonyl}-
cyclopentyl}methyl}-4-methoxybutanoic acid ; and
(*S*)-2-{{1-{{[2-(hydroxymethyl)-2,3-dihydro-1H-inden-2-yl]amino}carbonyl}-
cyclopentyl}methyl}-4-methoxybutanoic acid .

28 The method according to claim 1 wherein the female sexual dysfunction treated
30 includes at least female sexual arousal dysfunction (FSAD).

29 The method according to claim 1 wherein the medicament is administered
systemically.

35 30 The method according to claim 1 wherein the medicament is administered orally.

31 A method of treatment or prophylaxis of a condition for which a beneficial therapeutic response can be obtained by the inhibition of neutral endopeptidase comprising administration of a therapeutically effective amount of a compound as defined in claim 2.

5

32 A medicine comprising the compound of claim 2.

33 A pharmaceutical formulation including a compound as defined in claim 2 together with a pharmaceutically acceptable excipient.

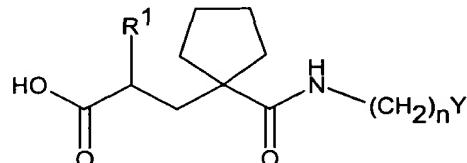
34 A method for the treatment or prophylaxis of female sexual dysfunction including administering to the patient a therapeutically effective amount of a compound as defined in claim 2.

15 35

A female sexual dysfunction pharmaceutical formulation including a therapeutically effective amount of a compound as defined in claim 2 together with a pharmaceutically acceptable excipient.

20 36

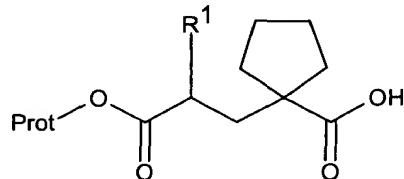
A process for preparing a compound of formula I or salts thereof



(I)

wherein R¹, n and Y are as defined in any one of claims 2 to 27, comprising the steps of:

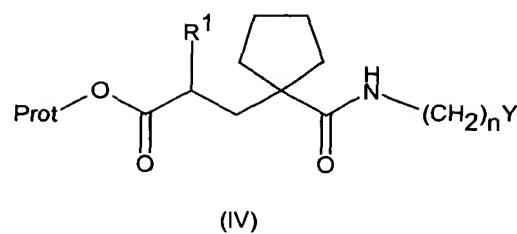
a) reacting a compound of formula II



(II)

25

wherein Prot is a suitable protecting group, with a compound of formula Y(CH₂)_nNH₂ (III), to give a compound of formula IV,



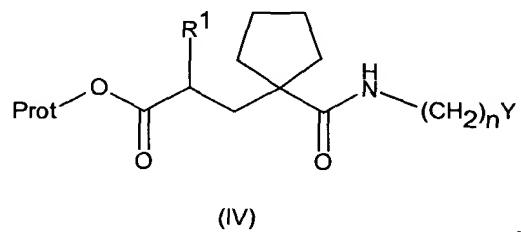
(IV)

;

then

5 b) reacting the compound of formula IV under suitable deprotecting conditions to give the compound of formula I; then
c) optionally forming a salt.

37. A compound of formula IV



(IV)

,

10

wherein R^1 , n , and Y are as defined in claim 2 and wherein Prot is a protecting group.